NOT FOR PUBLICATION

UNITED STATES DISTRICT COURT
DISTRICT OF NEW JERSEY

CATALYST PHARMACEUTICALS, INC. AND SERB S.A., Plaintiffs, v. JACOBUS PHARMACEUTICALS COMPANY, INC., Defendant.	Civil Action No. 20-14590 (MAS) (DEA) **MEMORANDUM OPINION**
CATALYST PHARMACEUTICALS, INC. AND SERB S.A., Plaintiff, v. PANTHERX SPECIALTY, LLC, AND PANTHER SPECIALTY HOLDING, CO., Defendants.	Civil Action No. 20-17040 (MAS) (DEA) **MEMORANDUM OPINION**

SHIPP, District Judge

This matter comes before the Court upon Defendants' Jacobus Pharmaceutical Company, Inc. ("Jacobus"), Pantherx Specialty, LLC and Panther Specialty Holding, Co. ("Pantherx") (collectively "Defendants") Motion to Dismiss Plaintiffs' Catalyst Pharmaceuticals, Inc. ("Catalyst") and SERB S.A. ("SERB") (collectively "Plaintiffs") Complaints ((No. 20-14590, Jacobus Compl., ECF No. 1) and (No. 20-17040, Pantherx Compl., ECF No. 1)) pursuant to

Federal Rule of Civil Procedure 12(b)(6). (ECF No. 33.)[1] Plaintiffs filed Opposition (ECF No. 39) and Defendants filed a Reply (ECF No. 47). The Court has carefully considered the parties' submissions and decides the matter without oral argument pursuant to Local Civil Rule 78.1. For the reasons set forth below, Defendants' Motion to Dismiss is DENIED.

I. BACKGROUND

A. Factual History

The following facts are drawn from the Complaints and taken as true for purposes of this Memorandum Opinion. Plaintiff Catalyst is a corporation organized under the laws of the State of Delaware with its principal place of business at 355 Alhambra Circle, Suite 1250, Coral Gables, Florida, 33134. (Ja. Compl. ¶¶ 2–3; Px. Compl. ¶¶ 2–3.) Plaintiff SERB is a corporation organized under the laws of Belgium with its principal place of business at 480 Avenue Louise, Brussels, 1050 Belgium. (Ja. Compl. ¶ 3; Px. Compl. ¶ 3.) Defendant Jacobus is a New Jersey corporation having a place of business at 37 Cleveland Lane, Princeton, New Jersey, 08540. (Ja. Compl. ¶ 7.) Defendant Pantherx Specialty LLC is a limited liability company incorporated in the state of Pennsylvania having a place of business at 24 Summit Park Drive, Pittsburgh, Pennsylvania, 15275. (Px. Compl. ¶ 7.) Defendant Panther Specialty Holding, LLC is a limited liability company incorporated in the state of Pennsylvania having a place of business at 24 Summit Park Drive, Pittsburgh, Pennsylvania, 15275. (*Id.* ¶ 8.) Pantherx Specialty LLC and Panther Specialty Holding, LLC (collectively "Pantherx") are affiliates who, together and in concert, do business under the fictitious names Pantherx Rare and Pantherx Rare LLC. (*Id.* ¶ 9.) In May 2019, Jacobus obtained approval from the FDA for Ruzurgi®, a pharmaceutical product approved to treat pediatric

[1] On January 21, 2021, the Court consolidated both cases for all purposes. (Jan. 21, 2021 Order, ECF No. 41.)

patients. (Ja. Compl. ¶¶ 31–35.) Pantherx is the exclusive specialty pharmacy for filling Ruzurgi® prescriptions in the U.S. (Defs.' Moving Br. 2.)

Catalyst is the exclusive licensee and SERB is the owner by assignment of U.S. Patent No. 10,793,893 ("the '893 patent"). (Ja. Compl. ¶¶ 3–5; Px. Compl. ¶¶ 3–5.) Plaintiffs allege that Defendants have induced infringement of the '893 patent by knowingly and intentionally promoting and encouraging administration of Ruzurgi® to patients. (*See generally* Ja. Compl.; Px. Compl.)

B. The Patent

The '893 patent relates to methods of administering 3,4-Diaminopyridine ("3,4-DAP") also known as amifampridine. U.S. Patent No. 10,793,893. Amifampridine is useful in treating amifampridine-sensitive diseases, such as Lambert-Eaton Myasthenic Syndrome ("LEMS"), a rare and debilitating neuromuscular disorder involving impairment of neuromuscular transmission and serious muscle weakness. (*See generally* Ja. Compl.; Px. Compl.) Plaintiffs aver that the inventors of the '893 patent discovered that amifampridine undergoes acetylation in the body and that the acetylation rate of amifampridine varies significantly depending on certain genetic differences. (Ja. Compl. ¶ 20; Px. Compl. ¶ 21.) Variants of the N-acetyltransferase gene 2 ("NAT2") result in fast, intermediate, or slow acetylation of amifampridine. (*See* Ja. Compl. ¶ 38; Px. Compl. ¶ 30.) Plaintiffs assert that the inventors further discovered that amifampridine could be more safely and efficaciously administered by accounting for these individual genetic differences in acetylation rates among patients treated with amifampridine-sensitive diseases, such as LEMS. (Ja. Compl. ¶ 38; Px. Compl. ¶ 30.)

The '893 patent contains fifteen claims, one of which is independent. '893 Patent col. 90:5-52. Independent claim 1 of the '893 patent recites:

> A method of treating a human patient diagnosed with a 3,4-diaminopyridine (3,4-DAP) sensitive disease in need of treatment thereof comprising administering a dose of about 2.5 mg to about 30 mg of 3,4-DAP or a pharmaceutically acceptable salt thereof to a human patient who is a slow acetylator having an N-acetyl transferase 2 (NAT2) gene comprising: a C282T mutation on both alleles of the NAT2 gene; a T341C mutation on both alleles of the NAT2 gene; or a C282T mutation on one allele of the NAT2 gene and a T341C mutation on the other allele of the NAT2 gene.

'893 Patent col. 90:5–14.

C. Plaintiffs' Complaints

Plaintiffs assert that Defendants actively induce infringement of at least claim 1 of the '893 patent by knowingly and intentionally promoting and encouraging administration of Ruzurgi® to patients with LEMS who are slow acetylators of amifampridine, including patients having the specific genetic mutations listed in claim 1 in violation of 35 U.S.C. § 271(b). (Ja. Compl. ¶¶ 39–43, 45, 53; Px. Compl. ¶¶ 31–35, 37, 45.)

II. LEGAL STANDARD

Under Federal Rule of Civil Procedure 12(b)(6), a complaint may be dismissed for "failure to state a claim upon which relief can be granted." A complaint fails to state a claim under Rule 12(b)(6) if it does not allege "enough facts to state a claim to relief that is plausible on its face." *Bell Atl. Corp. v. Twombly*, 550 U.S. 544, 570 (2007). "Where a complaint pleads facts that are 'merely consistent with' a defendant's liability, it stops short of the line between possibility and plausibility of 'entitlement to relief.'" *Ashcroft v. Iqbal*, 556 U.S. 662, 678 (2009) (internal quotation marks omitted). When considering plausibility, "courts accept all factual allegations as true, construe the complaint in the light most favorable to the plaintiff, and determine whether, under any reasonable reading of the complaint, the plaintiff may be entitled to relief." *Fowler v. UPMC Shadyside*, 578 F.3d 203, 210 (3d Cir. 2009) (quoting *Phillips v. Cnty. of Allegheny*, 515 F.3d 224, 233 (3d Cir. 2008)).

III. DISCUSSION

A. Parties' Positions

Defendants move to dismiss Plaintiffs' Complaints in their entirety, and with prejudice under Federal Rule of Civil Procedure 12(b)(6) for failure to state a claim, asserting two arguments. (*See generally* Defs.' Moving Br., ECF No. 33–1.) Defendants first argue that the Complaints should be dismissed because the '893 patent is invalid under 35 U.S.C. § 101 ("§ 101") for lack of patent-eligible subject matter. (*Id.* at 3, 24–25.) Defendants also argue that the '893 patent fails to claim a "specific" method of treatment, and therefore the claims are directed to a natural phenomenon. (Defs.' Moving Br. 31–32 (citing *Vanda Pharms. Inc. v. West-Ward Pharms. Int'l Ltd.*, 887 F.3d 1117, 1136 (Fed. Cir. 2018).) Second, Defendants argue that the Complaints should be dismissed because the Complaints allege no plausible claim of induced infringement against them. (Defs.' Moving Br. 3, 33–40.)

Conversely, Plaintiffs argue that Defendants fail to prove as a matter of law that the claims are directed solely to patent ineligible subject matter. (Pls.' Opp'n Br. 2, ECF No. 39.) Plaintiffs argue that the claims are not directed to a mere natural phenomena or abstract idea because they use 3,4-DAP "to treat a specific medical condition (severe muscle weakness) in a specific patient population (patients who are slow 'acetylators' (i.e., metabolizers) of 3,4-DAP) using a modified treatment regimen (lowering the dose of 3,4-DAP based on the rate of metabolization)." (Pls.' Opp'n Br. 2.) Plaintiffs argue that the Complaints plead specific factual allegations putting Defendants on notice of Plaintiffs' induced infringement theories and provide specific facts in support thereof. (Pls.' Opp'n Br. 3–4, 22–27.)

As explained more fully below, the Court finds that Defendants' arguments with respect to 35 U.S.C. § 101 are more appropriate for consideration upon a more fully developed factual record. In addition, Plaintiffs have stated a claim for induced infringement.

B. Patentability under 35 U.S.C. § 101

Section 101 of the Patent Act provides, "[w]hoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title." 35 U.S.C. § 101. Section 101, however, has an implicit limitation: laws of nature, natural phenomena, and abstract ideas are not patentable. *Mayo Collaborative Servs. v. Prometheus Lab'ys, Inc.*, 566 U.S. 66, 70 (2012) (internal quotation marks and citation omitted). The Supreme Court has set forth a two-step analysis to determine whether a claim is patent-eligible under § 101 in the *Mayo* and *Alice* decisions. *Mayo*, 566 U.S. at 77–79; *Alice Corp. Pty. v. CLS Bank Int'l*, 573 U.S. 208, 217 (2014). "First, we determine whether the claims at issue are directed to one of those patent-ineligible concepts[,]" i.e. laws of nature, natural phenomena, or abstract ideas. *Alice*, 573 U.S. at 217. Second, the additional elements of the claim are considered both "individually and 'as an ordered combination' to determine whether the additional elements 'transform the nature of the claim' into a patent-eligible application." *Id.* (quoting *Mayo*, 566 U.S. at 78). This second step is described as "a search for an inventive concept—i.e., an element or combination of elements that is sufficient to ensure that the patent in practice amounts to significantly more than a patent upon the [ineligible concept] itself." *Id.* (citing *Mayo*, 566 U.S. at 72–73) (internal quotation marks omitted). To establish that particular claims are invalid, a party must overcome a patent's presumption of validity under 35 U.S.C. § 282 by clear and convincing evidence. *Data Distrib. Techs., LLC v. BRER Affiliates, Inc.*, No. 12-4878, 2014 WL 4162765, at *5 (D.N.J. Aug. 19,

2014). Further, "[i]f the Court is going to invalidate . . . on subject matter eligibility grounds before claim construction, then [d]efendants must establish that the only plausible construction" renders the claimed subject matter ineligible with no factual inquiries. *Id.* at *6 (internal quotation marks and citation omitted).

1. *Alice/Mayo* Step One

Defendants argue that the claims of the '893 patent are "'directed to' the . . . natural phenomenon of how the body metabolizes 3,4-DAP through the naturally-occurring, naturally-polymorphic NAT2 enzyme." (Defs.' Moving Br. 26.) Defendants assert that "the claims are not directed to a novel, improved method of treatment" for three reasons. (*Id.*) First, the treatment elements and prior art dosages of the claims are not "new" or "innovative." (*Id.*) Second, Plaintiffs "cannot point to any innovation other than [the] purported discovery of the natural law." (*Id.* (internal quotation marks omitted).) Finally, the method fails to "propose a new way of treating . . . patients that leverages this discovery." (*Id.* (internal quotation marks and emphasis omitted).) In support, Defendants offer an interpretation of the term "total daily dose" in claim 6 and an interpretation of dosages in claims 1 through 5 based on their lack of incorporation of this term. (*Id.* at 8–9.) This portion of the argument indicates the need for claim construction prior to a § 101 analysis as argued by Plaintiffs. (*See* Pls.' Opp'n Br. 12, 30 ("'[w]ithout claim construction, agreement between the parties, proposals from Plaintiff, or an evidentiary record, the Court cannot assume the meaning of' necessary claim terms to determine a motion to dismiss under § 101." (quoting *Data Distrib.*, 2014 WL 4162765, at *13)).) The Federal Circuit also noted that claim construction, while not an inviolable prerequisite to a validity determination under § 101, "will ordinarily be desirable—and often necessary—to resolve claim construction disputes prior to a § 101 analysis . . . ." *Bancorp Servs., L.L.C. v. Sun Life Assur. Co. of Canada (U.S.)*, 687 F.3d

1266, 1273–74 (Fed. Cir. 2012). Defendants' argument, however, also suffers from another deficiency. As noted by Plaintiffs, Defendants' argument raises many underlying factual issues regarding the novelty of the claimed treatment elements and dosages compared to the prior art (an inquiry under 35 U.S.C. § 102). (*See generally* Pls.' Opp'n Br.)

Plaintiffs argue that (1) *Mayo* is distinguishable and that (2) the '893 patent's method-of-treatment claims are patentable under the Federal Circuit's *Classen* and *Vanda* decisions. (Pls.' Opp'n Br. 13–20 (citing *Classen Immunotherapies, Inc. v. Biogen IDEC*, 659 F.3d 1057 (Fed. Cir. 2011); *Vanda*, 887 F.3d at 1117).) First, Plaintiffs argue that the claims of the '893 patent satisfy § 101 because "they require the practical, active step of changing how 3,4 DAP is administered to a LEMS patient who is a slow acetylator" unlike the claims at issue in *Mayo* which merely required physicians to "reconsider" changing the dosing regimen and lacked a concrete, active step. (Pls.' Opp'n Br. 18 (citing *Mayo*, 566 U.S. at 82).) Second, Plaintiffs argue that method of treatment claims are a long-recognized category of patent-eligible subject matter, and that the '893 patent's claims are nearly identical in material respect to the method-of-treatment claims held patentable in *Vanda*. (*Id.* at 3, 13–14 (citing *Classen*, 659 F.3d at 1066; *Vanda*, 887 F.3d at 1121).) Plaintiffs further argue that both the claims at issue in *Vanda* and the claims in the '893 patent leverage the underlying law of nature and are "directed to *methods of treating a patient*" in contrast to the *Mayo* claims which were "directed to a *diagnostic* method." (*Id.* at 14 (emphasis in original); *Vanda*, 887 F.3d at 1135.) Additionally, Plaintiffs point to two Federal Circuit cases finding that similar method-of-treatment claims were not "directed to" a patent ineligible concept at step one of the *Alice*/*Mayo* framework. (*Id.* at 18–19 (citing *Endo Pharm. Inc. v. Teva Pharm. USA, Inc.*, 919 F.3d 1347, 1351, 1353 (Fed. Cir. 2019); *Natural Alternatives Int'l, Inc. v. Creative Compounds, LLC*, 918 F.3d 1338, 1346, 1349 (Fed. Cir. 2019).)

In response, Defendants note that claim 1 of the '893 patent lacks two elements present in the *Vanda* claim. (Defs.' Reply Br. 9.) Defendants do not, however, demonstrate how these elements were relevant to the Federal Circuit's decision in favor of patent eligibility of the *Vanda* claim. (*See generally id.*) Given this failure, in addition to Defendants' raising of claim construction issues and factual issues surrounding the claimed treatment elements and dosages compared to the prior art novelty, this Court finds that Defendants do not demonstrate that "the only plausible construction" of the claims renders them patent ineligible under § 101. *Data Distrib.*, 2014 WL 4162765, at *6 (citation omitted). Since Defendants fail to show that the '893 patent claims are "directed to" patent ineligible subject matter under step one of the *Alice/Mayo* framework, this Court need not address step two of the *Alice/Mayo* inquiry. *Vanda*, 887 F.3d at 1134.

2. Specific Method of Treatment

Defendants argue that the '893 patent claims are not directed to a "specific method of treatment," "specific patients," or any "specific outcome," when they broadly recite treatment of "3,4-DAP sensitive diseases," and therefore the claims are directed to a natural phenomenon. (Defs.' Moving Br. 31 (citing *Vanda*, 887 F.3d at 1136).) Defendants argue that the patent's treatment of "3,4-DAP sensitive diseases" implicates a large and potentially limitless class, and, even if not, "there is nothing specific about the claimed disease, patients, or outcome" when "'[t]he therapeutically effective amount [of 3,4-DAP] will vary depending on the condition to be treated,' and the 'appropriate [3,4-DAP] dosage levels . . . for specific diseases and conditions' may yet 'emerge' as future 'studies are conducted.'" (*Id.* at 31–32 (citing '893 Patent, 8:14–20; 34:13–19; 39:35–44).)

Plaintiffs respond by arguing that the claims are not directed to a mere natural phenomena or abstract idea because they use 3,4-DAP "to treat a specific medical condition (severe muscle weakness) in a specific patient population (patients who are slow 'acetylators' (i.e., metabolizers) of 3,4-DAP) using a modified treatment regimen (lowering the dose of 3,4-DAP based on the rate of metabolization)." (Pls.' Opp'n Br. 2.) Further, Plaintiffs argue that the claims of the '893 patent provide novel solutions to an unknown and unexpected problem of accumulation of excess 3,4-DAP in slow acetylator patients which leads to increased adverse events. (*Id.* at 2–3.)

While Defendants may raise a legitimate question as to the breadth of the claims, the issue cannot be resolved without a factual inquiry. Therefore, whether the '893 patent claims are directed to a specific method of treatment is not appropriate for resolution as a matter of law on a motion to dismiss.

C. Induced Infringement

"Whoever actively induces infringement of a patent shall be liable as an infringer." 35 U.S.C. § 271(b). "To prove inducement, the patentee must show *direct infringement*, and that the alleged infringer *knowingly* induced infringement and possessed *specific intent* to encourage another's infringement." *i4i Ltd. P'ship v. Microsoft Corp.*, 598 F.3d 831, 851 (Fed. Cir. 2010) (emphasis added) (internal quotation marks and citation omitted). Inducement may be based on the labeling of a pharmaceutical that will lead at least some users to infringe the asserted method claims. *See AstraZeneca LP v. Apotex, Inc.*, 633 F.3d 1042, 1056–60 (Fed. Cir. 2010).

Defendants argue that Plaintiffs fail to "plausibly allege that the Ruzurgi® labeling induces administration of Ruzurgi® to 'slow acetylators' with the specific NAT2 mutations recited in the '893 patent Claims." (Defs.' Moving Br. 35–39.) Specifically, Defendants argue that Plaintiffs fail to plausibly allege each of the three elements of induced infringement. (*Id.*) First, Plaintiffs fail to

plausibly assert *direct infringement* by healthcare providers or patients with respect to the claimed mutations. (*Id.* at 36 (emphasis in original).) Second, Plaintiffs fail to plausibly show Defendants' *knowledge* of any use of Ruzurgi® meeting the claimed mutations or that such alleged use constitutes direct infringement. (*Id.* at 37 (citing *Commil USA, LLC v. Cisco Sys., Inc.*, 575 U.S. 632, 638-40 (2015).) Finally, Plaintiffs fail to plausibly allege that Defendants had the required *specific intent* to encourage healthcare providers' or patients' use of Ruzurgi® with respect to the claimed mutations. (*Id.*)

Defendants' arguments underlying each of the three elements of induced infringement are not persuasive because they hinge upon the assertion that the Ruzurgi® labeling does not specifically identify the claimed NAT2 mutations of claim 1 of the '893 patent. In the Complaints, however, Plaintiffs point to the "Pharmacogenomics" section of the Ruzurgi® Prescribing Information which, presumably, refers to the claimed mutations indirectly: "Genetic variants in the N-acetyltransferase gene 2 (NAT2) affect the rate and extent of RUZURGI metabolism. In normal healthy volunteers, poor metabolizers, also referred to as 'slow acetylators' (i.e., ***carriers of two reduced function alleles***) had higher average plasma amifampridine concentrations . . . ." (Ja. Compl. Ex. 3, at 11; Px. Compl. Ex. 2, at 11.) Thus, the slow acetylator, or poor metabolizer, NAT2 phenotype of the Ruzurgi® labeling arises from two genetic mutations within NAT2 referred to as "reduced function alleles."

The labeling does not explicitly identify these alleles as noted by Defendants. (*See generally* Defs.' Moving Br.) Defendants fail to show, however, that "two reduced function alleles" refers to mutations different from those claimed within the '893 patent. (*See generally* Defs.' Moving Br.; Defs.' Reply Br.) Thus, it is plausible to infer that "two reduced function alleles" refers to the specific NAT2 mutations claimed in the '893 patent. Even without this

inference, however, the label teaches administration of Ruzurgi® based upon NAT2 poor metabolizer status, as Plaintiffs allege. (Ja. Compl. ¶¶ 35–38; Px. Compl. ¶¶ 27–30.) Therefore, given the high frequency of the poor metabolizer phenotype within the population,[2] Defendants cannot reasonably assert a lack of knowledge of infringement or specific intent to induce infringement without at least providing evidence of some other genetic source of the poor metabolizer phenotype. Defendants fail to show any other genetic source of this phenotype.[3] (*See generally* Defs.' Moving Br.; Defs.' Reply Br.) Further, Defendants fail to cite legal authority requiring that the label expressly identify the specific mutations recited in the claims to promote infringement. (*See generally* Defs.' Moving Br.; Defs.' Reply Br.)

1. Direct Infringement

For present purposes, there appear to be four elements to claim 1. While the preamble of a claim is not generally limiting, in some instances it can limit the scope[4] of the claim. Considering the allegations in the Complaints in the light most favorable to Plaintiffs, the preamble could be considered to introduce the first element. The four elements considered here are (1) treating a human patient diagnosed with a 3,4-diaminopyridine (3,4-DAP) sensitive disease in need of treatment thereof, (2) administering a dose of about 2.5 mg to about 30 mg of 3,4-DAP or a

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[2] The Ruzurgi® Prescribing Information states that, within the general population, the "NAT2 poor metabolizer phenotype prevalence is 40-60% in the White and African American populations, and 10-30% in Asian ethnic populations." (Ja. Compl. ¶ 38 (citing Ja. Compl. Ex. 3, at 11); Px. Compl. ¶ 30 (citing Px. Compl. Ex. 2, at 11).)

[3] Defendants argue that during prosecution Applicants made admissions to the Patent Office that slow acetylators *can have* NAT2 alleles containing different mutations than those claimed in the '893 patent. (Defs.' Reply Br. 15 (citing Defs.' Moving Br. Ex. E, at 71).) Applicants did not make this specific admission. Rather, Applicants rebutted the Examiner's inherent anticipation rejection by arguing that the slow acetylator populations studied in the prior art references cited by the Examiner *could have had* NAT2 alleles containing different mutations than those claimed in the '893 patent.

[4] *See Shoes by Firebug LLC v. Stride Rite Children's Grp., LLC*, 962 F.3d 1362, 1368 (Fed. Cir. 2020) (". . . [U]se of preamble terms to define positive limitations in the body of claims can evince an inventor's intent that the preamble limit the scope of the claim.").

pharmaceutically acceptable salt thereof, (3) to a human patient who is a slow acetylator, and (4) [the patient] having an N-acetyl transferase 2 (NAT2) gene comprising: [the claimed NAT2 mutations]. (Ja. Compl. ¶ 22 (citing Ja. Compl. Ex. 1 at 85); Px. Compl. ¶ 22 (citing Px. Compl. Ex. 1 at 85).) Defendants do not dispute Plaintiffs' allegation of direct infringement of elements one or three. As noted above, Defendants' argument that Plaintiffs have failed to plausibly assert direct infringement because the label does not explicitly identify the claimed mutations (i.e. because the label lacks element four) fails because there is a reasonable inference that the Ruzurgi® label does identify the mutations. Plaintiffs, therefore, plausibly assert direct infringement of elements one, three, and four:

> On information and belief, physicians prescribing Ruzurgi® have administered, and will continue to administer, the drug to patients with LEMS who are slow acetylators of amifampridine, including patients having an NAT2 gene with a C282T mutation on both alleles, a T341C mutation on both alleles, or a C282T mutation on one allele and a T341C mutation on the other allele.

(Ja. Compl. ¶ 39; Px. Compl. ¶ 31.) Plaintiffs also assert element four:

> The recommended starting dosage of RUZURGI in pediatric patients weighing 45 kg or more **who are known N-acetyltransferase 2 (NAT2) poor metabolizers** is **15 mg** daily taken orally in divided doses. The recommended starting dosage in pediatric patients weighing less than 45 kg **who are known NAT2 poor metabolizers is 7.5 mg** daily taken orally in divided doses.

(Ja. Compl. ¶ 36 (emphasis added) (citing Ja. Compl. Ex. 3, at 3); Px. Compl. ¶ 28 (emphasis added) (citing Px. Compl. Ex. 2, at 3).) The recommended Ruzurgi® starting doses for known NAT2 poor metabolizers of 7.5 mg and 15 mg are within the "2.5 mg to about 30 mg of 3,4-DAP" dose range of claim 1. '893 Patent col. 90:8–11.

Defendants argue that nothing in the Ruzurgi® Labeling instructs physicians or patients to use the "doses" or "total daily doses" recited in the '893 patent claims. (*See generally* Defs.' Moving Br.) To make these arguments, however, Defendants repeatedly assert that the Ruzurgi®

labeling indicates that the physician use the "prior art" method of individualized titration. (*Id.*) Defendants also rely on the fact that total daily doses exceed the claimed range. (*Id.*) These arguments fail because in a plausible reading, claim 1 of the '893 patent claims at least one single dose within the 2.5 mg to 30 mg range as indicated by the claim terms "comprising"[5] and "a dose." '893 Patent col. 90:7. Thus, a titration method including single doses within the claimed range may be infringing. Similarly, a total daily dose exceeding the claimed range may infringe if it includes a single dose within the range. Thus, these arguments raise factual issues inappropriate for resolution at the pleadings stage.

Even if the inference that the Ruzurgi® label identifies the mutations were not plausible, Plaintiffs have plausibly alleged indirect infringement. To state a claim for indirect infringement, "a plaintiff need not identify a specific direct infringer if it pleads facts sufficient to allow an inference that at least one direct infringer exists." *In re Bill of Lading Transmission & Processing Sys. Pat. Litig.*, 681 F.3d 1323, 1336 (Fed. Cir. 2012). As noted above, Defendants have not proposed a genetic source of the poor metabolizer phenotype other than the claimed NAT2 mutations. (*See generally* Defs.' Moving Br.; Defs.' Reply Br.) Taking Plaintiffs' contention that physicians are treating LEMS patients with Ruzurgi® according to the instructions of the label as true in combination with the high frequency of the poor metabolizer phenotype within the population, it is plausible that at least one physician has administered Ruzurgi® to a LEMS patient having the claimed genetic mutations using the Ruzurgi® label's recommended starting dosage for poor metabolizers.

[5] "The transition 'comprising' in a method claim indicates that the claim is open-ended and allows for additional steps." *Invitrogen Corp. v. Biocrest Mfg., L.P.*, 327 F.3d 1364, 1368 (Fed. Cir. 2003).

2. Knowledge

The Supreme Court "clarified that the 'knowledge' required for inducement includes both knowledge of the patent and knowledge of infringement." *WAG Acquistion, LLC v. Multi-Media, LLC*, No. 14-1661, 2015 WL 5310203, at *8 (D.N.J. Sept. 10, 2015) (emphasis omitted) (citing *Commil USA, LLC v. Cisco Sys., Inc.*, 575 U.S. 632, 639 (2015)). Defendants do not argue a lack of knowledge of the patent, only that there is no knowledge of infringement. (Defs.' Moving Br. 37.) Defendants' argument focuses again on the assertion that nothing in the Ruzurgi® labeling shows knowledge by Defendants that patients taking Ruzurgi® will have the specifically claimed NAT2 mutations. (*Id.*) For the reasons stated above, there is a reasonable inference that Defendants do know that some patients will have the specifically claimed NAT2 mutations. Even if not, Defendants cannot claim a lack of knowledge of infringement given the high frequency of poor metabolizers in the population and Defendants' failure to at least show evidence of some other source of the phenotype. Defendants also argue that "nothing in the Ruzurgi® label instructs physicians to even investigate or determine whether patients have the claimed mutations." (*Id.*) Conversely, Plaintiffs argue that there is no genetic testing step recited in the claims. (Pls.' Opp'n Br. 24–25.) Plaintiffs further argue that the Ruzurgi® label strongly implies that doctors should determine a patient's acetylator status by using the phrase "known poor metabolizer" and recommending a dramatically different starting dose based on that acetylator status. (*Id.* at 25.) Defendants suggest that this argument is counterintuitive. (Defs.' Reply Br. 15.) It is not, however, implausible for a physician to infer that patients' acetylator status should be determined based on the Ruzurgi® label information cited by Plaintiffs. Thus, this Court finds that Plaintiffs have plausibly asserted Defendants' knowledge of infringement.

3. Specific Intent

"To prove inducement, the patentee must show . . . that the alleged infringer . . . possessed specific intent to encourage another's infringement." *i4i Ltd.*, 598 F.3d at 851 (internal quotation marks and citation omitted). Induced infringement "can be found where there is evidence of active steps taken to encourage direct infringement," such as "instructing how to engage in an infringing use." *Takeda Pharms. U.S.A. v. West-Ward Pharm. Corp.*, 785 F.3d 625, 630–31 (Fed. Cir. 2015) (internal quotation marks and citation omitted). "The question is not just whether instructions describe the infringing mode," but whether such instructions "evidence intent to encourage infringement" such that the Court is "willing to infer from those instructions an affirmative intent to infringe the patent." *Id.* at 631 (internal quotation marks and citation omitted).

Defendants argue that the Ruzurgi® label does not encourage "the use of Ruzurgi® specifically with patients having the claimed mutations."[6] (Defs.' Moving Br. 38.) As noted above, this argument fails, in part, because a plausible inference can be made that the "two reduced function alleles" of the Ruzurgi® label refer to the claimed mutations of the '893 patent and, even if not, Defendants cannot claim a lack of specific intent to induce infringement based on the label's lack of explicit reference to the mutations.

Defendants further argue that because the Ruzurgi® labeling merely allows for administration to known NAT2 poor metabolizers, Plaintiffs have failed to show inducement. (Defs.' Moving Br. 38 (citing *Ferring Pharms. Inc. v. Lupin Inc.*, No. 1:19-CV-913-RGA, 2020 WL 3414750, at *4 (D. Del. June 22, 2020); *Takeda.*, 785 F.3d at 632; *Shire, LLC v. Amneal Pharms., LLC*, No. 11-3781, 2014 WL 2861430, at *4–5 (D.N.J. June 23, 2014).) Plaintiffs argue

[6] Defendants also argue that Pantherx does not consider genetic mutations or acetylator status of patients when filling prescriptions for Ruzurgi® and therefore no plausible allegation of the necessary specific intent has been made. (Defs.' Reply Br. 12–13 n. 3.) Defendants failed to make this argument, however, when moving for dismissal, reserving it for the reply brief.

that the Ruzurgi® label "encourages doctors to administer the claimed doses and daily doses recited in the asserted claims" to poor metabolizers. (Pls.' Opp'n Br. 25–27.) In support of this argument, Plaintiffs point to the Ruzurgi® Prescribing Information which instructs that for "patients weighing 45 kg or more who are known N-acetyltransferase 2 (NAT2) poor metabolizers," the starting dose is "15 mg daily taken orally in divided doses." (*Id.* at 26 (quoting Ja. Compl. Ex. 3, at 3; Px. Compl. Ex. 2, at 3.) Thus, the prescribing information does more than merely describe an infringing mode; it teaches administration of a dose of Ruzurgi® within the claimed range to poor metabolizers.

Plaintiffs further support the inference of "specific intent" from the label by analogizing to *Vanda*. (Pls.' Opp'n Br. 26.) In *Vanda*, the court inferred specific intent to encourage the performance of a genotype test for poor metabolizer status from the following language:

> Approximately 7 to 10% of Caucasians and 3 to 8% of Black/African Americans lack the capacity to metabolize CYP2D6 substrates and are classified as poor metabolizers (PM), . . . PMs of CYP2D6 have higher exposure to iloperidone compared with [extensive metabolizers] and *PMs should have their dose reduced by one-half. Laboratory tests are available to identify CYP2D6 PMs.*

Vanda, 887 F.3d at 1131. Plaintiffs argue that the Ruzurgi label is materially indistinguishable from the label of *Vanda* in light of similar language in the Ruzurgi® label,[7] in combination with (1) the label's explanation that poor metabolizers have "two reduced function alleles" in NAT2 and (2) the label's starting dose instructions for known poor metabolizers. (Pls.' Opp'n Br. 26.)

[7] "40-60% [of] the White and African American populations, and . . . 10-30% [of the] Asian ethnic populations" are "poor metabolizers." (Pls.' Opp'n Br. 26 (quoting Ja. Compl. Ex. 3, at 10–11; Px. Compl. Ex. 2, at 10–11; *see* Ja. Compl. ¶ 38; Px Compl. ¶ 30).)

While the materiality of distinctions between *Vanda* and the present case is arguable,[8] Plaintiffs show a plausible inference of specific intent to induce infringement from the Ruzurgi® label. Conversely, Defendants fail to show that Plaintiffs have not plausibly alleged specific intent based on the label. It is unnecessary, therefore, to address Plaintiffs' argument that the Complaints allege more than just the label in support of induced infringement. (*Id.* at 27.)

IV. CONCLUSION

For the reasons discussed above, it is hereby ordered that Defendant's Motion to Dismiss is DENIED.

s/ Michael A. Shipp
MICHAEL A. SHIPP
UNITED STATES DISTRICT JUDGE

[8] Defendants' counter arguments focus mainly on arguments previously addressed. (Defs.' Reply Br. 14–15.) For example, Defendants argue that *Vanda* is distinguishable because the label at issue aligned with the claimed method of treatment which had two limitations for which there are no analogous limitations in the '893 patent, and that the Ruzurgi® label does not instruct specific therapeutic doses within the claimed ranges of the '893 patent. (*Id.*) Additionally, the *Vanda* language cited by Plaintiffs was important to the court drawing an inference about physicians genotyping patients, a limitation for which there is no analogue within the '893 patent. *Vanda*, 887 F.3d at 1131.